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2. Topol EJ, Gum P, Kottke-Marchant K. Determination of the natural history of aspirin resistance among stable patients with cardiovascular disease—Reply. *J Am Coll Cardiol* 2003;42:1336-7.

Angiotensin-Converting Enzyme Inhibitors, Beta-Blockers, and Mortality in Systolic Heart Failure

We read with interest the study by Johnson et al. (1). We believe that one of the key findings of this study was the relatively low rates of angiotensin-converting enzyme inhibitor (ACEI) angiotensin receptor blocker (ARB) and beta-blocker (BB) use in heart failure (HF) patients discharged from the hospital within three months, at 44.3% and 20.9%, respectively, from 1999 to 2000. Furthermore, only 11.3% of these patients received both an ACEI/ARB and a BB. The inclusion in this study of HF patients with preserved left ventricular systolic function (LVSF), or diastolic HF, may partially account for the low rates of utilization of these medications. The current American College of Cardiology/American Heart Association (ACC/AHA) HF guidelines do not have a recommendation to use either ACEI/ARB or BB in patients with diastolic HF. Lack of appropriate use of ACEI/ARB and BB in HF patients with impaired LVSF or systolic HF indicates poor quality of care and is clearly associated with poor outcomes. Although there is pathophysiological rationale for use of ACEI/ARB and BB in patients with diastolic HF (2), lack of use of these drugs in diastolic HF is neither poor quality of care nor is it associated with poor outcomes. We believe that HF quality improvement programs should focus on increasing the use of ACEI and BB in patients with systolic HF, and studies of quality and outcomes of HF care should classify patients based on their LVSF. Furthermore, ARBs are not currently recommended in systolic HF unless patients have an absolute contraindication to ACEI (2). The U.S. Centers for Medicare and Medicaid Services in its Seventh Scope of Work (2002 to 2005) identified use of ACEI, not ARB, as a quality indicator for HF care for Medicare beneficiaries (3).

We also note with interest an apparent lack of survival benefit of combined use of ACEI/ARB and BB on one-year mortality as compared to therapy with ACEI/ARB alone (1). Most large randomized controlled trials of BBs in systolic HF enrolled patients who were already receiving an ACEI. These studies showed that use of a BB resulted in an additional 35% reduction in mortality in subjects receiving both drugs compared with those receiving an ACEI alone (4). The rate of BB use in patients with systolic HF is low (5), and we are concerned that the finding of lack of survival benefit of BBs in HF as shown in the study by Johnson et al. (1) might be perceived by some clinicians as evidence that results of clinical trials do not necessarily translate into real-life patients.

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REFERENCES

1. Johnson D, Jin Y, Quan H, Cujec B. Beta-blockers and angiotensin-converting enzyme inhibitors/receptor blockers prescriptions after hospital discharge for heart failure are associated with decreased mortality in Alberta, Canada. *J Am Coll Cardiol* 2003;42:1438-45.
2. Hunt SA, Baker DW, Chin MH, et al. ACC/AHA guidelines for the evaluation and management of chronic heart failure in the adult: executive summary. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to revise the 1995 Guidelines for the Evaluation and Management of Heart Failure). *J Am Coll Cardiol* 2001;38:2101-13.
3. IPRO. Medicare National Health Care Quality Improvement Projects. Available at: http://www.ipro.org/index_pro_hcqip. Accessed on November 5, 2003.
4. Brophy JM, Joseph L, Rouleau JL. Beta-blockers in congestive heart failure. A Bayesian meta-analysis. *Ann Intern Med* 2001;134:550-60.
5. McMurray JJ, Ostergren J, Swedberg K, et al. Effects of candesartan in patients with chronic heart failure and reduced left-ventricular systolic function taking angiotensin-converting-enzyme inhibitors: the CHARM-Added trial. *Lancet* 2003;362:767-71.

REPLY

Drs. Thornton and Ahmed have identified one important message from our population cohort study (1). We agree that beta-blockers and angiotensin-converting enzyme (ACE) inhibitors/receptor blockers were underutilized in heart failure (HF) patients in Alberta, Canada (1), and elsewhere (2-5). We found that adjusted one-year mortality was lower in seniors hospitalized for HF who were prescribed beta-blockers (18.2%; 95% confidence interval [CI] 14.2 to 22.2) or ACE inhibitor/receptor blockers (22.3%; 95% CI 20.9 to 23.7) within three months of hospital discharge than in those with no prescriptions (29.9%; 95% CI 28.8 to 31.0). The use of both beta-blockers and ACE inhibitors/receptor blockers was associated with an even lower mortality (16.6%; 95% CI 13.3 to 20.0) than ACE inhibitor/receptor blockers alone (22.3%; 95% CI 20.9 to 23.7).

The underutilization of effective therapy is not unique (6) even for therapies such as these that have been repeatedly documented to be beneficial in clinical trials that span over a decade (7). To improve the utilization of beta-blockers and ACE inhibitors/receptor blockers, their utilization has been flagged as a marker of quality of care. Our study may provide some clues as to why underutilization persists. Heart failure is not defined in terms of preservation or loss of systolic function; rather, it is a clinical constellation of symptoms (8). Both systolic and diastolic impairment in HF are independently associated with increased mortality risk (9). Clinical trials are not representative of the general population with HF, as younger, male, white, and decreased ejection-fraction patients are over-represented (10). The use of the exclusion criteria of decreased ejection fraction has the effect of under-recruitment of older female patients. In Alberta, seniors (age 65 years and older) constituted about 85% of all new diagnoses for HF during the study period (April 1, 1994, to March 31, 1999). Hospitalized patients age 75 years and older constituted about 60% of all incident, prevalent, and total hospitalization cases during this study period. In those age 75 years and older, women constituted over 56% of hospitalized HF patients. The population in Alberta was similar to that noted in the United States (10).

Thus, the reflective clinician may quite rightly question whether clinical trial results are generalizable to the demographically different population of hospitalized HF patients. Our study can only associate decreased mortality to the use of beta-blockers and